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10/643,589

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Debra D. Pittman

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EXAMINER

EMCH, GREGORY S

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/643,589	Applicant(s) PITTMAN ET AL.	
	Examiner Gregory S. Emch	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,8-58 and 85-87 is/are pending in the application.
- 4a) Of the above claim(s) 32-41,45-58 and 85-87 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,8-31 and 42-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The finality of the last Office action is withdrawn, and new grounds of rejection are set forth below. The amendment filed on 06 February 2009 has been received and entered in full.

Response to Amendment

Claims 1, 20 and 43 have been amended, and claims 3-7 and 88-92 have been canceled as requested in the amendment filed on 06 February 2009. Following the amendment, claims 1, 8-58 and 85-87 are pending in the instant application.

In the reply filed on 06 February 2009, applicants traverse the withdrawal of claim 86, because applicants assert that said claim depends from claim 1 and relates to SEQ ID NO: 5 (a fusion protein of human RAGE- LBE and an Fc domain). Applicants assert that SEQ ID NO: 5 comprises amino acid residues 1 through 344 of SEQ ID NO: 7 (see, e.g., Figure 3A), thereby falling within the scope of amended claim 1. Thus, applicants request rejoinder of claim 86 with the elected invention.

Applicants' arguments have been fully considered and are not found persuasive. SEQ ID NO: 5 does not comprise residues 1 to 344 of SEQ ID NO: 7. For example, at residue 102, SEQ ID NO: 7 is Met, whereas residue 102 in SEQ ID NO: 5 is Asn. There are several other mismatches as well. Thus, Applicants' assertion is inaccurate and claim 86 will not be rejoined at this time. Applicants are reminded that they elected the species of SEQ ID NO: 7 without traverse.

Claims 32-41, 45-58 and 85-87 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the replies filed on 24 August 2006 and 23 July 2007.

Claims 1, 8-31 and 42-44 are under examination in the instant office action.

Formal Matters

Applicants' amendment to the sequence listing submitted on 11 September 2008 is acknowledged. In this amendment, applicants state, "Applicants have noted two errors in the Sequence Listing filed June 30, 2004. First, in SEQ ID NO: 6, 60 nucleotides were inadvertently left out at the position 135. Second, in SEQ ID NO: 7, lysine (K) at position 110 was inadvertently changed to histidine (H) in error. Applicants enclose herewith a substitute Sequence Listing to correct these errors. Support for the substitute Sequence Listing can be found in the application (e.g., Figures 3B and 7). No new matter has been introduced."

The amended sequence listing has been entered in full. Since position 110 is now correctly listed as lysine (K), the examiner's comments from the previous office action at p.8 are invalid. Here it was stated, e.g. "Thus, the mismatch at residue 110 shown in Sequence Alignment B disqualifies the Morser et al. patent as prior art for claims 3-7 and 88-92, because these claims require no mismatch at residue 110." The Morser et al. patent indeed teaches no mismatch at residue 110 of SEQ ID NO: 7, as evidenced by the amended sequence listing.

New issues are set forth below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8-11 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,864,018 to Morser et al. (issued 26 January 1999; filed 16 April 1996; citation AA on IDS dated 01 March 2004), and as evidenced by Neeper et al. (Cloning and expression of a cell surface receptor for advanced glycosylation end products of proteins. J Biol Chem. 1992 Jul 25;267(21):14998-5004).

The claims are directed to a fusion protein comprising a Receptor for Advanced Glycation End Product Ligand Binding Element (RAGE-LBE) and an immunoglobulin element, wherein the RAGE-LBE comprises amino acid residues 1 through 344 of SEQ ID NO: 7.

The Morser et al. patent teaches that polypeptides of the invention include RAGE polypeptides and those that are related to and/or derived from human RAGE polypeptides (col.5, lines 3-6). Although the patent does not explicitly recite the sequence information for full-length human RAGE, it inherently teaches such, since it teaches the term "RAGE polypeptide" (see e.g. col.2, lines 45-47; col.8, lines 7-14). Accordingly, this human RAGE polypeptide comprises amino acid residues 1-404 of

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SEQ ID NO: 7, and this sequence information was well known in the art at the time of filing, as evidenced by Neeper et al. (see p.15001, Figure 3). Thus, the Morser et al. patent inherently teaches a RAGE polypeptide, which is 100% identical to the instant SEQ ID NO: 7, and therefore meets the limitation of the RAGE-LBE comprising residues 1-344 of SEQ ID NO: 7, as in claim 1. The patent discloses fusion proteins comprising human RAGE polypeptides, and fragments, including but not limited to ligand binding elements, immunoglobulin-like domains and human sRAGE (col.4, lines 65-66), which comprises residues 1-340 of SEQ ID NO: 7 (see Morser et al. SEQ ID NO: 2). Further, the instant specification teaches that a peptide comprising residues 1-329 of RAGE also comprises Ig1, Ig2 and Ig3 domains (see Figure 5). Thus, given that the instant specification does not explicitly define the claimed "immunoglobulin element," broadest reasonable interpretation of "immunoglobulin element" is met by Morser et al. patent, since the patent teaches human RAGE, which inherently comprises the Ig1, Ig2, and Ig3 domains, i.e. immunoglobulin elements, as evidenced by applicant's Figure 5 which shows the location of these Ig domains. Applicants are reminded that chemical compounds and their properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA1963)), as are their processes and yields (*In re Von Schickh*, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). Therefore, as set forth above, the Morser et al. patent teaches the limitations of claims 1 and 8-10.

The patent discloses one or more amino acid substitutions, insertions, or deletions, i.e. point mutations, which cause altered specificity, enhanced potency, and higher affinity (col.8, line 43 – col.10, line 4), thus meeting the limitations of claim 11.

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The patent teaches pharmaceutical compositions comprising the polypeptides of the invention and a pharmaceutically acceptable carrier (col.19, lines 21-24; col.20, lines 12-20), thus meeting the limitations of claim 19. Since the patent teaches all the elements of the claims (both expressly and inherently), claims 1, 8-11 and 19 are anticipated by U.S. Patent No. 5,864,018 to Morser et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicants are advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,864,018 to Morser et al., and as evidenced by Neeper et al. as applied to claims 1, 8-11 and 19 above, and further in view of Peppel et al. (1991; citation U on PTO-892 dated 18 October 2007)

The claims are directed to a fusion protein comprising a Receptor for Advanced Glycation End Product Ligand Binding Element (RAGE-LBE) and an immunoglobulin element, wherein the RAGE-LBE comprises amino acid residues 1 through 344 of SEQ ID NO: 7.

The Morser et al. patent and Neeper et al. reference teach as set forth above. The difference between the disclosure of the Morser et al. patent and the claimed invention is that the patent does not teach a fusion protein comprising a RAGE-LBE and an immunoglobulin element that is not inherent to the structure of RAGE, e.g. a portion of an separate antibody fused to the RAGE-LBE.

However, upon reading the disclosure of the Morser et al. patent, the skilled artisan would have recognized the desirability of developing improved compositions for treating disorders that result from the association of AGEs and RAGE. Furthermore, the Peppel et al. reference teaches fusion proteins comprising a soluble extracellular

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receptor moiety (of TNF- α) linked to an immunoglobulin element, wherein the immunoglobulin element comprises the C_H2 and C_H3 domain of human IgG1, i.e. the Fc domain (p.1483, paragraph 3 – p.1484, paragraph 4), as in claim 13. The Peppel et al. reference teaches that the fusion protein is an effective inhibitor of the ligand-receptor interaction (entire document, e.g. abstract).

As evidenced by the Morser et al. patent, the skilled artisan would have known that the interaction between AGE and RAGE is implicated in numerous pathological disease states and that improved inhibitors of this interaction would be desirable. As evidenced by the Peppel et al. reference, the skilled artisan would have recognized the desirability creating a construct, which comprises a soluble extracellular receptor moiety linked to an Fc domain of an immunoglobulin for inhibiting a ligand-receptor interaction. Given that Morser et al. teach that RAGE-LBE fusion proteins are useful as inhibitors of AGE/RAGE interaction and given that Peppel et al. teach that an extracellular receptor moiety-Fc fusion protein is a desirable inhibitor for the ligand-receptor interaction, it would have been reasonable to predict that a fully functional fusion protein comprising the RAGE polypeptide disclosed Morser et al. and comprising the Fc fragment taught by Peppel et al. could be successfully produced. Thus, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to improve Morser et al.'s soluble RAGE fusion protein as disclosed by Peppel et al. to yield predictable results. This is because the artisan has good reason to pursue the known options within his or her technical grasp. Such would amount to a substitution of

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known equivalent elements, one fusion proteins for another, to obtain predictable results.

Claims 12-18, 20-31 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,864,018 to Morser et al., in view of Peppel et al. and as evidenced by Neeper et al. as applied to claims 1, 8-11, 13 and 19 above, and further in view of U.S. 20020102604 to Milne Edwards et al. (citation A on PTO-892 dated 26 September 2006; published 01 August 2002, filed 07 December 2000) and as evidenced by WO 94/10308 to Spriggs et al. (citation N on PTO-892 dated 26 September 2006; published 11 May 1994).

The claims are directed to a fusion protein comprising a Receptor for Advanced Glycation End Product Ligand Binding Element (RAGE-LBE) and an immunoglobulin element, wherein the RAGE-LBE comprises amino acid residues 1 through 344 of SEQ ID NO: 7; further comprising a dimerizing polypeptide (including an amphiphilic polypeptide), a purification polypeptide, a stabilizing polypeptide, or a targeting polypeptide, and associated protein complexes and pharmaceutical compositions that comprise a TNF- α inhibitor.

The Morser et al., Neeper et al. and Peppel et al. references teach as set forth above. The references fail to teach the remaining elements of the fusion proteins of claims 12-18, 20-31 and 42-44.

However, upon reading the disclosure of the Morser et al. patent, the skilled artisan would have recognized the desirability of developing improved compositions for

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treating disorders that result from the association of AGEs and RAGE, e.g., improved RAGE-LBE fusion proteins. Furthermore, U.S. 20020102604 to Milne Edwards et al. teaches fusion proteins comprising polypeptides of the invention and functional fragments thereof (paragraphs 0117, 0176 and 0230). The reference teaches antibodies and fragments thereof, (including heavy chains [VH], Fc domains and CH1 domains) as potential partners in the fusion proteins (para. 0364, 0376 and 0377), as in claims 12-16. The '604 application teaches that the fusions can comprise any combination of the above-mentioned antibody fragments or domains (para. 0376 and 0377), as in claim 16. The '604 application teaches dimerizing polypeptides, including leucine zippers, as part of the fusions proteins of the invention (para. 0312, 0313, 0314), as in claims 18, 20, 27 and 31. Also, at paragraph 314, the '604 application states "examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference." Accordingly, WO 94/10308 to Spriggs et al. teaches jun and fos leucine zippers (p.1, line 34 – p.2, line 2), as in claims 28 and 29. The '604 application teaches stabilizing polypeptides (1260), targeting polypeptides (para. 1679), and purification polypeptides (para. 0176) as part of the fusion proteins of the invention, as in claim 20. The '604 application to Milne Edwards et al. also teaches amphiphilic polypeptides and fragments as part of the fusion proteins (para. 1679), as in claim 21, and teaches that fragments of polypeptides can at least 6, at least 8 to 10, 12, 15, 20, 25, 30, 35, 40, 50, 60, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 350, 400, 450 or 500 amino acids (para. 0333), as in claims 22-25. The '604 application teaches a

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peptide helix bundle (para. 0671), as in claim 26, and teaches that formation of multimers (i.e., dimerization) can be the result of ionic interaction (i.e., oppositely charged polypeptides bound to each other; para. 0312), as in claim 30. The '604 document teaches protein complexes, comprising a protein of the invention (e.g., para. 0667), as in claim 42. The '604 document teaches TNF- α inhibitors (e.g., uromodulin) as part of pharmaceutical compositions of the invention (para. 0825), as in claims 43 and 44.

None of the cited references teach a fusion protein, wherein said immunoglobulin element comprises a CH1 domain of a first immunoglobulin class and a CH1 domain of a second immunoglobulin class, wherein the first and second immunoglobulin classes are not the same. However, in the instant case this is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize.

Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ (see MPEP § 2144.05). It would have been customary for an artisan of ordinary skill to determine the optimal immunoglobulin composition of the fusion protein of claim 17 by varying the immunoglobulin type in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of immunoglobulin type would have been obvious at the time of applicants' invention.

As evidenced by the Morser et al. patent, the skilled artisan would have known that the interaction between AGE and RAGE is implicated in numerous pathological disease states and that improved inhibitors of this interaction would be desirable. As

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evidenced by the Peppel et al. reference, the skilled artisan would have recognized the desirability creating a construct, comprising a soluble extracellular receptor moiety linked to an Fc domain of an immunoglobulin for inhibiting a ligand-receptor interaction. As evidenced by Milne Edwards et al. in view of Spriggs et al., the skilled artisan would have recognized the desirability of including the fusion proteins partners disclosed therein with RAGE-LBEs. Given that Morser et al. teach that RAGE-LBE fusion proteins are useful as inhibitors of AGE/RAGE interaction, given that Peppel et al. teach that an extracellular receptor moiety-Fc fusion protein is a desirable inhibitor for the ligand-receptor interaction and given that Milne Edwards et al. teach that the claimed fusion proteins partners are desirable, it would have been reasonable to predict that a fully functional fusion protein comprising the RAGE polypeptide disclosed Morser et al. and comprising the Fc fragment taught by Peppel et al. and comprising the other partners as taught by Milne Edwards et al. could be successfully produced.

Moreover, regarding the potential fusion proteins partners of the claims (other than the RAGE-LBE polypeptides), inclusion of said partners is clearly the result of routine optimization of parameters (MPEP § 2144.05). It would have been customary for an artisan of ordinary skill to determine the optimal fusion protein partner for inclusion with RAGE-LBE given both Peppel et al.'s and Milne Edwards et al.'s explicit teachings of how to design such. At the time of the invention, all of the reagents were readily available and the technology existed to prepare fusion proteins as claimed and Milne Edwards et al. had demonstrated success in producing fusion proteins with no loss of function and being useful for therapeutic purposes. Thus one skilled in the art

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could have readily modified the RAGE-LBE containing fusion proteins of Morser et al. by optimizing them for therapeutic use as taught by Peppel et al. and Milne Edwards et al. Absent some demonstration of unexpected results from the claimed parameters, this optimization of proteins would have been obvious at the time of applicants' invention. Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to improve Morser et al.'s soluble RAGE fusion protein as disclosed by Peppel et al. and Milne Edwards et al. to yield predictable results. This is because the artisan has good reason to pursue the known options within his or her technical grasp. Such would amount to a substitution of known equivalent elements, one fusion proteins for another, to obtain predictable results.

In the reply filed on 06 February 2009, applicants assert that Morser et al. disclose fusion proteins comprising RAGE polypeptides and fragments thereof. Applicants assert that the RAGE-LBE disclosed in Morser et al. is only 340 amino acids in length and Morser et al. do not teach or suggest the human RAGE-LBE comprising residues 1-344 of SEQ ID NO: 7, as recited in claims 1, 20 or 43. Applicants assert that none of the other cited references bridge the gap between Morser et al. and the claimed invention. Applicants assert that the combination of cited references still fails to provide any suggestion or motivation for a skilled artisan to modify Morser's RAGE polypeptides to arrive at the claimed RAGE-LBE fusion proteins. Applicants assert that Morser provides no teaching or suggestion that RAGE polypeptides need to be further modified to improve their suitability or efficacy for any application. Applicants assert that there is

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no common connection between these cited disclosures that would have motivated a person skilled in the art to combine these teachings to make the RAGE-LBE fusion proteins as claimed.

Applicants' arguments have been fully considered and are not found persuasive. As set forth above, the Morser et al. patent teaches that polypeptides of the invention include RAGE polypeptides and those that are related to and/or derived from human RAGE polypeptides (col.5, lines 3-6). Although the patent does not explicitly recite the sequence information for full-length human RAGE, it inherently teaches such, since it teaches the term "RAGE polypeptide" (see e.g. col.2, lines 45-47; col.8, lines 7-14). Accordingly, this human RAGE polypeptide comprises amino acid residues 1-404 of SEQ ID NO: 7, and this sequence information was well known in the art at the time of filing, as evidenced by Neeper et al. (see p.15001, Figure 3). Thus, the Morser et al. patent inherently teaches a RAGE polypeptide, which is 100% identical to the instant SEQ ID NO: 7, and therefore meets the limitation of the RAGE-LBE comprising residues 1-344 of SEQ ID NO: 7, as in claim 1.

As stated previously, applicants' assertions that there is no suggestion or motivation to combine the cited references and arrive at the claimed invention is inaccurate. The motivation to combine can be found in the Morser et al. patent and the Peppel et al. reference. Specifically, the Morser et al. patent teaches that inventive compositions can comprise soluble RAGE polypeptides, i.e. fragments of RAGE that lack the transmembrane or cytoplasmic domains, and methods of using these compositions in screening, therapeutic and diagnostic applications, e.g. as blocking

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agents to inhibit or otherwise reduce the AGE/RAGE (ligand/receptor) interaction (col.4, line 58 - col.5, line 2). Furthermore, the Peppel et al. reference teaches that truncated receptor molecules, i.e. fragments that lack the transmembrane or cytoplasmic domains, are capable of interacting with TNF and can act as antagonists of TNF and as reagents to be used in defining the interaction between TNF and its receptor (ligand/receptor). The Peppel et al. reference teaches the desirability (e.g. increased stability and ease of purification) of engineering a chimeric protein in which the extracellular domain of the receptor, which normally engages the ligand, is covalently linked to IgG immunoglobulin domains (p.1483). Therefore, as evidenced by the Morser et al. patent, the skilled artisan would have known that developing fusion proteins comprising RAGE ligand binding fragments would be desirable. Furthermore, it would have been reasonable to predict that a fusion protein model taught by the Peppel et al. reference, i.e. an extracellular or soluble portion of a receptor linked to an immunoglobulin element, could be successfully used as the fusion protein model for the Morser et al. compositions comprising RAGE-LBE fusion proteins. Applicants' assertion that there is no nexus established between the prior art references of record is inaccurate. This is because a fusion protein comprising an extracellular or soluble portion of a TNF receptor as taught by Peppel et al. is analogous to a fusion protein comprising an extracellular or soluble portion of the RAGE receptor as taught by Morser et al.

Regarding applicants' assertion that Morser provides no teaching or suggestion that RAGE polypeptides need to be further modified, the fusion proteins are taught as

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potentially useful in providing for enhanced expression of the RAGE polypeptide constructs, or in producing RAGE polypeptides having other desirable properties, e.g., labeling groups, e.g., enzymatic reporter groups, binding groups, antibody epitopes, etc. This general disclosure of potential uses for the fusion proteins of Morser et al. would motivate the artisan to search the art for more specific polypeptides for inclusion with said fusion proteins. At the time of the invention, all of the reagents were readily available and the technology existed to prepare fusion proteins as claimed and Milne Edwards et al. and Peppel et al. had demonstrated success in producing fusion proteins with no loss of function and being useful for therapeutic purposes. It would have been customary for an artisan of ordinary skill to determine the optimal fusion protein partner for inclusion with RAGE-LBE given Peppel et al.'s and Milne Edwards et al.'s explicit teachings of how to design such. Thus one skilled in the art could have readily modified the RAGE-LBE containing fusion proteins of Morser et al. by optimizing them for therapeutic use as taught by Peppel et al. and Milne Edwards et al. Moreover, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose (MPEP §2144.07). Thus, contrary to applicants' assertions, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to improve Morser et al.'s soluble RAGE fusion protein as disclosed by Peppel et al. and Milne Edwards et al. to yield predictable results. This is because the artisan has good reason to pursue the known options within

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his or her technical grasp. Such would amount to a substitution of known equivalent elements, one fusion proteins for another, to obtain predictable results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/G.E./

Gregory S. Emch, Ph.D.

Patent Examiner

Art Unit 1649

15 March 2009

/Daniel E. Kolker/

Primary Examiner, Art Unit 1649

March 16, 2009